Spotlight on Bladder and Prostate Cancer and Urinary Retention at Glasgow Gathering

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The annual meeting of the British Association of Urologic Surgeons (BAUS) took place on the banks of the River Clyde, once the site of numerous shipyards in the golden age of shipbuilding in Glasgow. The city, with its world-renowned university, proved to be a magnificent setting for this year's meeting, opened by BAUS president R. Fletcher Deane, FRCSEd, FRCSGlas. The scientific sections, divided into 8 moderated podium sessions and 14 moderated poster sessions, covered all relevant topics of modern urology. In addition, the meeting was highlighted by 3 outstanding BAUS guest lecturers—Mr David Thomas, Dr Tom Stuttaford, and Dr Alan Wein—daily teaching courses and Internet sessions, and satellite symposia sponsored by pharmaceutical companies.

Bladder Cancer

An interesting study comparing the outcomes of transitional cell carcinoma (TCC) and squamous cell carcinoma (SCC) came from Peracha and colleagues[1] from the King Faisal Specialist Hospital and Research Center in Riyadh, Saudi Arabia. In contrast to most Western countries, in this series of 156 patients, the main histology was TCC in 89 patients (57%) and SCC in 67 patients (43%). While pathologic stages were relatively equally distributed between both main histologic groups, lymph node positivity occurred in 29% versus 14%, and *Bilharzia* eggs were found in 28% versus 17% of specimens with TCC versus SCC, respectively. Local tumor recurrence was noted in 27% versus 13.5%, respectively. The median survival was 2.7 years for patients with TCC and 3.2 years for those with SCC; the overall 5- and 10-year survival was 38% and 26% in the TCC group and 37% and 19% in the SCC group. In this interesting series, the occurrence of SCC was only a little lower than that of TCC, and the overall survival of patients with SCC and TCC was equivalent following cystectomy. This experience is unique, and most urologists practicing in Western countries will never see as many cases of SCC. It is, however, comforting to note that these patients stand just as good a survival chance if treated by radical cystectomy or cystoprostatectomy.

Mills and associates[2] asked whether meticulous pelvic lymphadenectomy for bladder cancer was justified. They reviewed data on 452 patients who underwent pelvic lymphadenectomy and cystectomy for bladder cancer. Node-positive disease was found in 83 patients (18%). The median overall survival was 20 months, with a 3- and 5-year survival of 38% and 30%, respectively. While the median survival for 57 patients with fewer than 5 positive nodes was 35 months, it was only 16 months for 26 patients who had 5 or more positive nodes ($P = .03$). Even more striking was the difference in median survival for 26 patients in whom the lymph node capsule was not perforated (93 months), compared with 57 patients in whom the cancer had perforated the lymph node capsule (16 months). The authors concluded that long-term survival was possible with node-positive bladder cancer; however, others found that patients do best if they have a limited number of nodes involved and if the cancer has not yet penetrated the capsule of the lymph nodes. A meticulous lymphadenectomy is suggested—if not for cure, then at least for proper counseling of the patient regarding prognosis.

Intravesical chemotherapy was addressed by several groups. A single-center experience with 123 patients who had biopsy-proven carcinoma in situ (CIS) was presented by Griffiths

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and coworkers[3] (from Newcastle upon Tyne, UK). Patients were divided into those with primary CIS only, CIS with concomitant or previous pTa TCC, and CIS associated with concomitant or previous pT1 TCC. All patients underwent a standard course of 6 weekly BCG instillations. Sixteen (53%) of 30 patients who did not respond received a second course of BCG, and 4 patients (13%) underwent radical cystectomy. Outcomes at 5 years are shown in the Table. Although complete response to BCG among patients in group 3 was associated with later progression and prolonged cancer-specific survival, only 30% of the patients were alive with bladders intact at 5 years. Thus, in patients with CIS and concomitant or previous pT1 TCC, a single course of BCG is inadequate, in the opinion of the authors, and maintenance BCG for those with a complete response or early radical cystectomy for nonresponders remains an alternative strategy.

Molecular markers remain of great interest in the field of TCC of the bladder and its treatment. A group from Newcastle upon Tyne suggested that stratification of patients based on staining for *p21(WAF1)* and *TP53* allows the separation of 4 distinct groups, with those overexpressing both markers having the best prognosis (3-year survival following radical radiotherapy of 82%), compared with those with a *p21(WAF1)*-negative and *TP53*-positive status (only 12% survival at 3 years).[4] The other combinations of staining fell somewhere between the 2 groups.

Bartlett and colleagues[5] from the Royal Infirmary in Glasgow performed fluorescence in situ hybridization (FISH) in primary bladder tumors from 54 patients and focused on chromosomes 7, 9, and 17. They found that chromosomal abnormalities occurred almost exclusively in primary tumors from 20 (63%) of 32 patients who had subsequent recurrence. Conversely, in patients with no recurrence, only 9% had chromosomal changes ($P < .001$). This exciting finding suggests that the analysis of primary TCC by FISH can predict recurrence with a positive predictive value of 91.3% and a sensitivity of 62.5%.

Benign Prostatic Hyperplasia

Several groups investigated issues surrounding incomplete or complete urinary retention. Bates and coworkers[6] from Exeter, UK, followed prospectively, for a median of 54 months, 93 men aged 40 to 84 years with a mean postvoid residual urine of 360 mL. The measured residual urine amounts remained stable in 51%, decreased in 29%, and increased in 20%. One third of all patients proceeded to transurethral resection of the prostate (TURP) at a mean follow-up time of 30 months, because of increased creatinine levels (n = 2), complete retention of urine (n = 7), increasing amounts of residual urine (n = 8), or worsening of symptoms (n = 14). The authors could not find a difference in initial flow rate, voided volume, or residual urine between those patients who developed complications and those who did not. There were no factors that could be used to predict which patients eventually would require surgery, and delaying surgery did not appear to jeopardize a positive outcome. This study adds to our limited knowledge regarding the natural history of residual urine, a parameter characterized by a significant intraindividual variability over time.

Other investigators (from Harrow, UK) examined the management of acute urinary retention after discharge from the emergency department, with a special emphasis on quality of life.[7] Of 101 patients presenting to the emergency department with acute retention, 83% were sent home after catheterization; 93% of those completed a questionnaire. Reported complaints included urinary leakage (46%), transient hematuria (44%), urgency (42%), pain around the penis (42%), painful erections (31%), and catheter blockage (27%). Twelve percent of the patients considered prolonged catheterization very inconvenient, yet 92% said they would find it acceptable to have a catheter in the future, if needed. A successful voiding trial was conducted in 46% of these patients. While the authors concluded that the quality of life for patients discharged with a catheter is not significantly impaired and that a period of catheterization before surgery does not increase the risk of perioperative

Table
5-Year Outcomes Following BCG Therapy for Bladder TCC

Stage	Alive/intact bladder (%)	Progression-free survival (%)	Cancer-specific survival (%)
CIS only	54	76	85
CIS + pTa TCC	56	86	94
CIS + pT1 TCC	30	41	58

TCC, transitional cell carcinoma; CIS, carcinoma in situ.

Main Points

- Meticulous lymphadenectomy is suggested for patients with bladder cancer to determine the number of nodes involved and the extent of node capsule penetration.
- Analysis of primary transitional cell carcinoma by fluorescence in situ hybridization has a positive predictive value of recurrence of 91.3%.
- Prostate-specific antigen assays can be misleadingly high in the acute phase of urinary retention.
- Transurethral electrovaporization of the prostate can be as effective as transurethral resection of the prostate in patients with moderate benign prostatic hyperplasia.
- In patients whose prostate cancer is managed by orchiectomy or hormonal androgen ablation, follow-up surveillance should include observation for bone loss.

complications, it would appear from a review of their data that nearly half of all patients responded affirmatively regarding any and all side effects associated with an indwelling catheter. Thus, while it probably is prudent to give all such patients a voiding trial, the remaining patients most likely should be referred to surgery relatively urgently, since indwelling catheters appear to be associated with considerable side effects and nuisance.

A practical question was asked by McNeill and colleagues[8] from the Western General Hospital in Edinburgh. These authors sought to evaluate the reliability of prostate-specific antigen (PSA) levels in the detection of cancer in patients presenting with acute urinary retention. Fifty-seven patients, all of whom had a clinically benign prostate on digital rectal examination, formed the study cohort. A PSA assay taken on admission was available for 54 patients. Prostatectomy was the choice for 35 patients, while the majority of the remaining patients had at least a biopsy for tissue diagnosis. Five of the 54 patients had prostate cancer; in 2, the PSA level was in the 0 to 4 ng/mL range, and in 3, more than 20 ng/mL. Histologic analysis revealed a prostatic infarction in only 11% of the prostatectomy specimens, while 74% had changes indicating prostatitis. The authors recommended avoiding PSA assays in the acute phase of urinary retention because the assays can be misleadingly high in this situation. For example, even with a threshold of 20 ng/mL, the assay's positive predictive value was no better than 17%. However, the issue that is not addressed is how long to wait after an episode of acute urinary retention before performing a PSA test. Further, it is difficult to counsel a young patient presenting in retention and failing a voiding trial. Most certainly, the patient would like to know more about the status of his prostate before proceeding with a prostatectomy. Yet, PSA levels are unreliable, and it is unclear how long it takes for these levels to return to normal baseline. This is an area in which additional research is needed.

Foley and associates[9] from Portsmouth, UK, reported the final data from their hematuria and benign prostatic hyperplasia (BPH) study. In this investigation, all patients presenting with hematuria caused only by BPH were entered into a prospective, randomized study to receive finasteride or no intervention. All patients were followed for 1 year, and the incidence of bleeding was recorded. In patients with no further bleeding after 1 year, finasteride was stopped, and they were followed for another year. The number of patients who were found to bleed at 3, 6, and 12 months in the control and finasteride groups were, respectively, 15 and 1, 16 and 3, and 16 and 4. After stopping finasteride, half the patients rebled within 6 months. The authors concluded that bleeding associated with BPH is a significant problem; if untreated, more than 60% of patients rebleed, and more than 30% will require surgical therapy. The researchers recommend finasteride in this setting, because it significantly reduces the incidence of rebleeding. However, finasteride treatment would have to be continued nearly indefinitely, since termination of treatment leads to an increased tendency to rebleed. A multicenter, randomized, placebo-controlled trial is needed to shed more light on this important issue.

Two groups reported on a trial of transurethral electrovaporization of the prostate (TUVP) versus TURP. In the study from Sunderland, UK, 53 patients with BPH were randomized to receive either TURP or TUVP.[10] The maximum flow rate (Q_{max}) increased from 8.8 to 19.6 mL/s at 12 months following TURP, and from 10.0 to 22.0 mL/s in the TUVP group. The mean voiding pressure at Q_{max} decreased from 83 to 48 cm H_20 in the TURP group and from 71 to 47 cm H_20 in the TUVP group. The authors concluded that there were no detectable differences between the 2 groups regarding these outcomes data and that both treatment modalities are effective methods to manage bladder outlet obstruction in patients with BPH.

The group from the Whipps Cross Hospital in London reported data on a randomized study comparing TURP with TUVP in 104 patients.[11] At 3 years' follow-up, the International Prostate Symptoms Score was reduced to 7.1 and 4.1 points, respectively, for TURP and TUVP; maximum flow rates were 18.0 and 22.2 mL/s, respectively, for the 2 groups. Reoperation rates were 4% in the first and second years and 5% during the third year, in both arms of the study. The authors concluded that TUVP is as effective and safe as standard TURP in the management of moderate BPH.

The investigators from New Zealand

(Fraundorfer and Gilling)[12] who first described the holmium laser enucleation of the prostate reported their favorable experience in 145 consecutive patients, and investigators from Derby, UK,[13] concurred in stating that holmium laser resection is safer than TURP, with a shorter hospital stay and convalescence, and provides a better quality of surgical care for patients with BPH.

Prostate Cancer

A topic of increasing concern is that of osteoporosis in prostate cancer patients. In men, hypogonadism may be associated with osteoporosis; after orchiectomy or hormone ablation, patients may experience severe bone loss. A cross-sectional study was undertaken of 48 men (mean age, 74.5 years) with locally advanced or metastatic prostate cancer who were treated with orchiectomy or hormonal androgen ablation.[14] Bone density was measured in the study group and compared with measurements in a control group of 110 men living in the community (mean age, 78 years). Bone densitometry in the patients with prostate cancer showed that 44% had T values of less than −2.5—which is the level suggested in the World Health Organization (WHO) guidelines for diagnosis of osteoporosis—and 31%, between −2.5 and −1.0, fulfilling the WHO guidelines for diagnosis of osteopenia. The authors (from London) concluded that hormonal deprivation may result in clinically significant bone loss and that this issue should not be overlooked in the surveillance of these patients.

An update on this type of treatment was given by D. Kirk on behalf of the MRC (Medical Research Council) Prostate Cancer Working Investigations group.[15] The question the investigators asked was whether hormonal treatment caused toxicity and excess deaths from conditions other than cancer. Of 934 patients enrolled in the study, 780 had died; 270 deaths were recorded from causes other than prostate cancer. Of the 270, 146 were in an immediate-hormonal-ablation group, while 124 were in a deferred-treatment group. In the immediate-treatment group, 51% of deaths not from cancer were ascribed to cardiovascular disease, compared with 71% in the deferred-treatment group. These data, therefore, are not consistent with the notion that early hormonal therapy causes an increase in cardiovascular mortality. This fact notwithstanding, the excess of death *not from prostate cancer* in the immediate-treatment group is of concern. It is expected that the MRC will present a detailed analysis of these patients in a future presentation or publication.

The group from Charing Cross Hospital in London presented their data on radical retropubic prostatectomy at 2 sessions. One presentation provided data on 177 consecutive patients undergoing radical retropubic prostatectomy who were analyzed for biochemical disease-free survival.[16] Remission was defined as a serum PSA level of 0.05 ng/mL or less. Unfortunately, 27% of the patients had to be excluded because they were lost to follow-up. Of the remaining 129 patients, 50 (39%) had biochemical failure. The majority of these patients (n = 40) did not achieve remission; ie, the PSA level never became undetectable. In the 10 patients who exhibited biochemical failure and achieved remission, relapse occurred after observation.

The second presentation of this group focused on external beam radiotherapy to the prostatic bed in patients who had a biochemical recurrence following radical prostatectomy.[17] A total of 28 men (16% of the total cohort) underwent external beam radiotherapy to the prostate bed; 3 of this group had metastatic disease within the pelvic lymph nodes. Following radiotherapy, the serum PSA level returned to less than 0.1 ng/mL in 79%, while it rose to higher than 0.1 ng/mL in 6 men who had been treated additionally with hormonal manipulation. Side effects were minimal, and mild proctitis occurred in 5 patients. The authors concluded that biochemical failure is common in their experience and is more likely to occur in patients with histologically positive margins. External beam radiotherapy to the prostate bed is successful in reversing the rise in PSA level, but such a reversal is less likely in those patients with nodal metastases. Furthermore, one has to question the durability of the response in serum PSA. Other investigators have found that while an initial reversal of the PSA level can be induced by external beam radiotherapy, most of these patients eventually will exhibit a rise again. It is clear that new strategies need to be developed to prevent PSA biochemical failure by better patient selection or by early intervention in patients selected based on negative predictive criteria.

Urinary Tract Stone Disease

Endourologists and physicians involved in the management of urinary tract stone disease are increasingly concerned with the indiscriminate use of shock wave lithotripsy (SWL) for all upper tract stones. Specifically, SWL alone has relatively low success rates in patients presenting with lower-pole caliceal stones, justifying the use of percutaneous nephrostolithotomy in such patients. Keeley and associates[18] reported on studies by 2 groups (from Western General Hospital in Edinburgh and Southmead Hospital in Bristol, UK) that addressed this topic. Both groups assessed the effect of the infundibular pelvic angle on stone regrowth or recurrence after SWL. Their SWL database was searched for patients with single lower-pole stones who had a regrowth or recurrence of stones; this group of patients was compared with a group followed for at least 4 years with no recurrence. The investigators identified 15 patients with regrowth or recurrence and 19

patients with no regrowth (mean follow-up, 6.1 years). Significant factors associated with regrowth were an acute infundibular pelvic angle and caliceal dilation (both, $P < .05$); insignificant factors were original stone-free status and infundibular diameter and length. The authors recommended considering both the infundibular pelvic angle and the degree of dilation before choosing a mode of therapy.

The group from Newcastle upon Tyne reviewed 62 patients who had undergone SWL for a solitary lower-pole caliceal stone.[19] Measurements that were taken included the infundibular pelvic angle; the infundibular vertical angle; the infundibular width and length; and the calyx-to-pelvis height, which is the distance between the horizontal line taken from the inferior aspect of the lower-pole calyx and the apex of the lower lip of the renal pelvis. Overall, the stone-free rate was 59%, while 17% of patients had no change in stone burden and 24% had fragments of less than 4 mm. Quite in contrast to the group from Bristol, these authors found no association between the type of calyx, the infundibular pelvic angle, the length of the infundibulum, or the stone size and treatment outcomes. The only measurements that were of significant value in predicting outcomes were the infundibular width and the calyx-to-pelvis height.

While on the surface these 2 abstracts seem to be contradictory, they asked 2 distinctly different questions, and the variance in outcomes might be caused by the patient population as well as the stratification. A multicenter lower-pole stone study group is currently examining this issue and other issues surrounding the utility of SWL and percutaneous nephrostolithotomy in patients with solitary lower-pole renal stones. We eagerly await the results.

Summary

The 1999 BAUS meeting provided a well-rounded and -balanced overview of current issues in the field of urology. The quality of the presentations spoke well for the high scientific standard at which urology is practiced in the United Kingdom. This is particularly evidenced in certain disease areas in which the National Health Service and the associated databases allow investigators unique insight into practice patterns and outcomes. This type of information is not available in the United States. ■

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